E. Resolution Test Mixture (RTM)

1.0-ml of the Codeinone/14-Hydroxycodeinone stock solution I was pipetted into a 50-ml volumetric flask. Using a micropipette, 100 µl of the unspiked Oxycodone solution was transferred and diluted to volume with ~0.85% phosphoric acid solution H. The concentration of Codeinone, 14-Hydroxycodeinone, and Oxycodone was approximately 100 ppm.

F. Sample Preparations

i. 50 mg/mL Oxycodone HCl Sample Solution

500±5 mg of Oxycodone HCl was weighed, in duplicate, into separate 10-mL volumetric flasks for each of Examples 1, 2 and 3. The Oxycodone HCl was then diluted to volume with the ~0.85% phosphoric acid solution II and swirled to dissolve the sample. A sufficient amount of this sample was transferred to an HPLC vial for injection.

G. HPLC Conditions

The HPLC conditions were set as follows:

TABLE 4

HPLC Conditions

Parameter	Condition
HPLC Column	Symmetry C_{18}, 3.0 × 150 mm, 3.5 µm particle size
Mobile Phase	18 mM phosphate/13 mM SDS pH = 7.50:ACN:MeOH (72.25:15.75:12.0) pH = 7.80 ± 0.01
Flow Rate*	0.7 mL/min
Column Temperature	40° C.
Detection	220 nm
Injection Volume	5 µL
Run Time	50 minutes

*Parameter may be adjusted to achieve retention times.

H. System Suitability

One injection (5-µL) of a blank solution (~0.85% phosphoric acid solution II) was made, followed by one injection of the RTM to determine if there was any interfering peaks in the blank solution. 6 injections of the working standard III were made. The system suitability injections were then tested to verify that they met the system suitability criteria as shown in Table 2.

TABLE 5

System Suitability Criteria

Parameter	Acceptance Criteria
Resolution between Codeinone and 14-Hydroxycodeinone	NLT 8
Resolution between 14-Hydroxycodeinone and Oxycodone	NLT 2
Tailing factor for Oxycodone	0.7-2.0
Relative retention times for Codeinone based on Oxycodone	Approx. 0.44
Relative retention times for 14-Hydroxycodeinone based on Oxycodone	Approx. 0.85
% RSD of 6 system suitability injections for Codeinone and 14-Hydroxycodeinone	NMT 20%

The expected retention times were as follows:

Components	Expected Retention Times
Codeinone	14 ± 2 min
14-Hydroxycodeinone	27 ± 4 min
Oxycodone	32 ± 6 min

I. Injection Procedure

Once the column was equilibrated, the sample and standard solutions were injected according to the following sequence of Table 3:

TABLE 6

Blank (diluent)	1 injection
Resolution solution	1 injection
Working Standard III	6 injections for RSD, last 2 injections for calibration
Blank (diluent)	2 injections
Unspiked Oxycodone solution	2 injections
Sample 1 Prep #1	2 injections
Working Standard III	2 injections
Sample 1 Prep #2	2 injections
Sample 2 Prep #1	2 injections
Sample 2 Prep #2	2 injections
Working Standard III	2 injections
Sample 3, Prep #1	2 injections
Sample 3, Prep #2	2 injections
Working Standard III	2 injections

The Codeinone and 14-Hydroxycodeinone peaks were identified using the relative retention times as discussed above.

Calculations

The responses of Codeinone and 14-Hydroxycodeinone peaks were measured and recorded. The content of Codeinone and 14-Hydroxycodeinone was calculated in ppm using the following equation:

$$\text{ppm} = \frac{Rs \times Wstd}{Rstd \times Ws} \times \frac{1}{100} \times \frac{1}{50} \times \frac{1}{10} \times \frac{10}{1} \times \frac{1{,}000{,}000}{1}$$

$$\text{ppm} = \frac{Rs \times Wstd \times 200}{Rstd \times Ws}$$

Where:

ppm=Parts per millions of codeinone or 14-Hydroxycodeinone in Oxycodone HCl

Rs=Response of Codeinone or 14-Hydroxycodeinone in Sample Solution.

Rstd=Response of Codeinone or 14-Hydroxycodeinone in Standard Solution minus the response of unspiked standard

Wstd=Weight of Standard, corrected for purity, mg

Ws=Weight of Sample, mg

1000000=Conversion Factor for ppm

% Codeinone/14-hydroxycodeinone=ppm/10,000

The results for Example 1 utilizing the procedure of Example 6 gave a result of <5 ppm of codeinone and 8 ppm of 14-hydroxycodeinone.

The results for Example 2 utilizing the procedure of Example 6 gave a result of <5 ppm of codeinone and <5 ppm of 14-hydroxycodeinone.

The results for Example 3 utilizing the procedure of Example 6 gave a result of <5 ppm of codeinone and 10 ppm of 14-hydroxycodeinone.

Many other variations of the present invention will be apparent to those skilled in the art and are meant to be within the scope of the claims appended hereto.

What is claimed is:

1. An oxycodone HCl composition comprising oxycodone HCl and 8α,14-dihydroxy-7,8-dihydrocodeinone, wherein the ratio of 8α,14-dihydroxy-7,8-dihydrocodeinone to oxycodone HCl is 0.04% or less as measured by HPLC.